Supporting Information #1

for

Cycloadditions of 1,1-Disubstitued Benzocyclobutenes Obtained by $C(sp^3)$ -H Activation

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General: Reactions were performed in oven-dried glassware under a positive pressure of argon. They were magnetically stirred and employed rubber septa. Reactions were monitored by thin layer chromatography (TLC) with SDS 0,25 mm silica gel 60 F254, by NMR or GC/MS. TLC plates were visualized by exposure to UV light (254 nm) or stained with *p*-anisaldehyde, potassium permanganate, ninhydrin or ammonium molybdate. All chemicals were purchased from commercial vendors and used as is, unless otherwise specified. Flash column chromatography was performed using normal phase silica gel (60 Å, 40–63 µm, Merck). Chemical shifts (δ) are quoted in parts per million (ppm) and are reported relative to chloroform for ¹H NMR (δ = 7.26 ppm) and for ¹³C NMR (δ = 77.16 ppm). ¹⁹F NMR spectra were calibrated with CCl₃F as external reference. NMR attributions were based on HMQC, HMBC, and COSY correlations. Data are reported as follows: chemical shift, multiplicity (s = singulet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet and br = broad), coupling constant in Hz, integration, attribution. GC/MS analysis was performed with simultaneous double injection on a DB-5ms column lined with a mass Electronic Impact (EI) or an FID detection system. Infrared spectra were recorded using a FT-IR instrument. High-resolution mass spectra were recorded on an ElectroSpray Ionisation (ESI) spectrometer.

Representative cycloaddition procedure:

A mixture of the benzocyclobutene (1 equiv.), the dienophile (1.5-2.0 equiv.) and *o*-dichlorobenzene (c = 1 mol/L) was placed in a closed vessel and irradiated at 250W max. in a focused microwave reactor for 15-20 min (temperature after 2-3 min: 180°C, external IR probe). The resulting mixture was directly purified by flash chromatography using first heptanes then heptanes and ethyl acetate as the eluent.

<u>1. Cycloaddition of 1,1-disubstituted BCB¹ 2a-k and N-methylmaleimide 4a (Table 1)</u>



The cycloaddition reaction was performed according to the standard procedure, starting from benzocyclobutene **2a** (40.5 mg, 0.230 mmol, 1 equiv.) and *N*-methylmaleimide (51.0 mg, 0.460 mmol, 2 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C for 15 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 8/2), product **5aa** was isolated as a colorless oil (61 mg, 0.21 mmol, 93% yield).

¹**H** NMR (300 MHz, CDCl₃): $\delta = 7.33-7.26$ (m, 2H, *H2*, *H3*), 7.21 (ddd, J = 7.0, 7.0, 2.0 Hz, 1H, *H4*), 7.09 (d, J = 7.0 Hz, 1H, *H5*), 3.82 (d, J = 8.6 Hz, 1H, *H11*), 3.62 (s, 3H, *H9*), 3.43 (ddd, J = 8.6, 8.6, 1.8 Hz, 1H, *H12*), 3.15 (dd, J = 15.6, 1.8 Hz, 1H, *H13*), 2.72-2.64 (m, 4H, *H13'*, *H16*), 1.99 (s, 3H, *H10*) ppm;

¹³C NMR (75 MHz, CDCl₃): $\delta = 179.1 (C15), 176.9 (C14), 175.4 (C8), 137.1 (C6), 134.0 (C1), 128.5 (C5), 128.1 (C2), 127.8 (C4), 125.5 (C3), 53.2 (C9), 48.9 (C7), 47.0 (C11), 40.2 (C12), 29.7 (C13), 24.8 (C16), 20.8 (C10) ppm;$

IR (film): $v = 2985 (v_{C-H}), 2992, 1724 (v_{C=O}), 1696 (v_{C=O}), 1432, 1247, 1106, 984, 768, 628 cm⁻¹;$ **HRMS (ESI):** $calculated for <math>C_{16}H_{17}NO_4^{23}Na^+ [M+Na]^+$: 310.1055, found: 310.1046.

¹ Chaumontet, M.; Piccardi, R.; Audic, N.; Hitce, J.; Peglion, J.-L.; Clot, E.; Baudoin, O. J. Am. Chem. Soc. **2008**, 130, 15157.



The cycloaddition reaction was performed according to the standard procedure, starting from benzocyclobutene **2b** (55 mg, 0.27 mmol, 1 equiv.) and *N*-methylmaleimide (59 mg, 0.53 mmol, 2 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C for 20 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 8/2), product **5b** was isolated as a white solid (67 mg, 0.21 mmol, 79% yield).

Mp: 128-129°C;

¹**H NMR (500 MHz, CDCl₃):** δ = 7.21 (d, *J* = 8.5 Hz, 1H, *H5*), 6.78 (dd, *J* = 8.5, 2.5 Hz, 1H, *H4*), 6.64 (d, *J* = 2.3 Hz, 1H, *H2*), 3.78 (d, *J* = 9.0 Hz, 1H, *H11*), 3.74 (s, 3H, *H17*), 3.61 (s, 3H, *H9*), 3.40 (ddd, *J* = 9.0, 8.3, 1.8 Hz, 1H, *H12*), 3.09 (dd, *J* = 15.5, 1.8 Hz, 1H, *H13*), 2.69 (s, 3H, *H16*), 2.65 (dd, *J* = 15.5, 8.3 Hz, 1H, *H13'*), 1.95 (s, 3H, *H10*) ppm;

¹³C NMR (75 MHz, CDCl₃): δ = 179.1 (C15), 177.0 (C14), 175.6 (C8), 159.2 (C3), 135.3 (C6), 129.1 (C1), 126.6 (C5), 114.0 (C2), 112.8 (C4), 55.2 (C17), 53.1 (C9), 48.3 (C7), 47.1 (C11), 40.2 (C12), 29.9 (C13), 24.8 (C16), 20.9 (C10) ppm;

IR (film): $v = 2955 (v_{C-H})$, 1730 $(v_{C=0})$, 1693 $(v_{C=0})$, 1498, 1385, 1247 (v_{C-0}) , 1050, 739 cm⁻¹; **HRMS (ESI):** calculated for $C_{17}H_{19}NO_5Na^+[M+Na]^+$: 340.1161, found: 340.1149.



According to the standard cycloaddition procedure, benzocyclobutene **2c** (40 mg, 0.17 mmol, 1 equiv.) was reacted with *N*-methylmaleimide (39 mg, 0.34 mmol, 2 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 9/1), product **5c** was isolated as a colorless oil (54 mg, 0.15 mmol, 91% yield).

¹**H** NMR (500 MHz, CDCl₃): $\delta = 6.82$ (s, 1H, *H5*), 6.60 (s, 1H, *H2*), 3.87 (s, 3H, *H17*), 3.82 (s, 3H, *H18*), 3.77 (d, J = 8.6 Hz, 1H, *H11*), 3.62 (s, 3H, *H9*), 3.39 (dd, J = 8.6, 8.6 Hz, 1H, *H12*), 3.06 (d, J = 16.4 Hz, 1H, *H13*), 2.71 (s, 3H, *H16*), 2.61 (dd, J = 16.4, 8.6 Hz, 1H, *H13*'), 1.98 (s, 3H, *H10*) ppm; ¹³C NMR (75 MHz, CDCl₃): $\delta = 179.3$ (C15), 177.0 (C14), 175.4 (C8), 148.5 (C4), 148.2 (C3), 129.0 (C1), 126.3 (C6), 111.6 (C2), 109.2 (C5), 56.0 (C17 or C18), 55.9 (C17 or C18), 53.1 (C9), 48.6 (C7), 47.1 (C11), 40.4 (C12), 29.3 (C13), 24.9 (C16), 21.0 (C10) ppm;

IR (film): $v = 2948 (v_{C-H})$, 2838, 1717 ($v_{C=O}$), 1693 ($v_{C=O}$), 1512, 1433, 1216 (v_{C-O}), 1017, 1103, 983, 792 cm⁻¹;

HRMS (ESI): calculated for $C_{18}H_{22}NO_6^+$ [M+H]⁺: 348.1447, found: 348.1441.

Product 5d



According to the general cycloaddition procedure, benzocyclobutene 2d (42 mg, 0.22 mmol, 1 equiv.) was reacted with N-methylmaleimide (48 mg, 0.43 mmol, 2 equiv.) in o-dichlorobenzene (175 µL) at 180 °C for 15 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 95/5), product 5d was isolated as a white solid (57 mg, 0.19 mmol, 87% yield).

Mp: 150-151°C;

¹**H NMR (500 MHz, CDCl₃):** δ = 7.29 (dd, J = 8.7, 5.5 Hz, 1H, H5), 6.95 (ddd, J = 8.7, 8.7, 2.7 Hz, 1H, H4), 6.83 (dd, J = 8.7, 2.7 Hz, 1H, H2), 3.81 (d, J = 9.3 Hz, 1H, H11), 3.62 (s, 3H, H9), 3.42 (ddd, J = 9.3, 8.1, 1.7 Hz, 1H, H12), 3.13 (dd, J = 15.6, 1.7 Hz, 1H, H13), 2.70 (s, 3H, H16), 2.66 (dd, J = 15.6, 8.1 Hz, 1H, H13'), 1.98 (s, 3H, H10) ppm;

¹³C NMR (75 MHz, CDCl₃): δ = 178.8 (C15), 176.7 (C14), 175.1 (C8), 162.3 (d, J = 247.9 Hz, C3), 136.3 (d, J = 7.8 Hz, CI), 132.9 (d, J = 3.4 Hz, C6), 127.3 (d, J = 7.8 Hz, C5), 115.6 (d, J = 21.4 Hz, C2), 114.5 (d, J = 21.4 Hz, C4), 53.2 (C9), 48.5 (C7), 46.9 (C11), 40.0 (C12), 29.7 (d, J = 1.3 Hz, *C13*), 24.9 (*C16*), 21.0 (*C10*) ppm;

¹⁹F NMR (282 MHz, CDCl₃): δ = -114.14 ppm;

IR (film): $v = 2925 (v_{C-H}), 1697 (v_{C=O}), 1494, 1381 (v_{C-F}), 1049, 738 \text{ cm}^{-1};$ **HRMS (ESI):** calculated for $C_{16}H_{15}NO_4F^{-1}[M-H]^{-1}$: 304.0985, found: 304.0994.



The cycloaddition reaction was performed according to the general procedure, starting from benzocyclobutene 2e (33 mg, 0.14 mmol, 1 equiv.) and N-methylmaleimide (30 mg, 0.27 mmol, 2 equiv.) in o-dichlorobenzene (200 µL) at 180 °C for 20 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 8/2), product 5e was isolated as a white solid (39 mg, 0.11 mmol, 81% yield). Cristals suitable for X-ray diffraction analysis were grown from heptanes. Crystallographic data for this compound have been deposited with the Cambridge Crystallographic Data Centre under CCDC 707911.

Mp: 134-135°C

¹**H NMR (300 MHz, CDCl₃):** $\delta = 7.56$ (d, J = 8.0 Hz, 1H, H4), 7.46 (d, J = 8.0 Hz, 1H, H5), 7.38 (s, 1H, H2), 3.86 (d, J = 8.9 Hz, 1H, H11), 3.64 (s, 3H, H9), 3.47 (ddd, J = 8.9, 8.2, 1.8 Hz, 1H, H12), 3.23 (dd, J = 15.8, 1.8 Hz, 1H, H13), 2.73 (s, 3H, H16), 2.72 (dd, J = 15.8, 8.2 Hz, 1H, H13'), 2.04 (s, 3.14 Hz), 2.04 (s, 33H, *H10*) ppm;

¹³C NMR (75 MHz, CDCl₃): δ = 178.6 (*C*15), 176.5 (*C*14), 174.6 (*C*8), 141.1 (*C*1), 135.0 (*C*6), 130.4 (q, J = 32.6 Hz, C3), 126.3 (C5), 125.3 (q, J = 3.5 Hz, C2), 124.9 (q, J = 3.5 Hz, C4), 123.9 (q, J = 271.8 Hz, C17), 53.4 (C9), 49.1 (C7), 46.7 (C11), 39.9 (C12), 29.7 (C13), 25.1 (C16), 20.9 (C10) ppm; ¹⁹F NMR (282 MHz, CDCl₃): δ = -62.52 ppm;

IR (film): $v = 2985 (v_{C-H}), 1718 (v_{C=O}), 1693 (v_{C=O}), 1435, 1328 (v_{C-F}), 1077, 618 \text{ cm}^{-1};$ **HRMS (ESI):** calculated for $C_{17}H_{15}NO_4F_3$ [M-H]⁻: 354.0953, found: 354.0970.



X-ray crystal structure of compound **5e** (30% ellipsoid plot)



The cycloaddition reaction was performed according to the standard procedure, starting from pyridocyclobutene **2f** (41 mg, 0.21 mmol, 1 equiv.) and *N*-methylmaleimide (48 mg, 0.43 mmol, 2 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C for 15 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 8/2), product **5f** was isolated as a white solid (41 mg, 0.14 mmol, 79% yield).

Mp: 135-136°C;

¹**H NMR (300 MHz, CDCl₃):** δ = 8.54 (d, *J* = 5.1 Hz, 1H, *H4*), 8.34 (s, 1H, *H2*), 7.24 (d, *J* = 5.1 Hz, 1H, *H5*), 4.18-4.04 (m, 2H, *H9*), 3.85 (d, *J* = 9.0 Hz, 1H, *H11*), 3.49 (ddd, *J* = 9.0, 8.2, 1.8 Hz, 1H, *H12*), 3.20 (dd, *J* = 15.6, 1.8 Hz, 1H, *H13*), 2.72 (s, 3H, *H16*), 2.66 (dd, *J* = 15.6, 8.8 Hz, 1H, *H13'*), 1.98 (s, 3H, *H10*), 1.13 (t, J= 7.1 Hz, 3H, *H17*) ppm;

¹³C NMR (75 MHz, CDCl₃): δ = 178.5 (*C15*), 176.4 (*C14*), 173.3 (*C8*), 149.8 (*C4*), 148.8 (*C2*), 146.3 (*C1*), 129.6 (*C6*), 120.3 (*C5*), 62.4 (*C9*), 48.7 (*C7*), 46.4 (*C11*), 39.8 (*C12*), 26.4 (*C16*), 25.0 (*C13*), 20.1 (*C10*), 13.9 (*C17*) ppm;

IR (film): $v = 2940 (v_{C-H})$, 1724 $(v_{C=O})$, 1685 $(v_{C=O})$, 1430, 1279, 1220, 1103, 989 cm⁻¹; **HRMS (ESI):** calculated for $C_{16}H_{19}N_2O_4^+ [M+H]^+$: 303.1345, found: 303.1333.

Synthesis of benzocyclobutene 2g



Concentrated sulfuric acid (8.70 mL, 163.4 mmol, 10 equiv.) was added dropwise to a stirred solution of 2-(2-bromo-4,5-dimethoxyphenyl)acetonitrile (4.18 g, 16.3 mmol, 1 equiv.) in MeOH (60 mL) at 0°C. The mixture was then refluxed for 4 d. After cooling, water was added and the mixture was extracted with CH_2Cl_2 . The combined extracts were washed with brine, dried (MgSO₄) and the solvent removed under reduced pressure to afford the methyl ester (4.42 g, 15.3 mmol, 93 % yield) that was used without further purification.

¹H NMR (300 MHz, CDCl₃): δ = 7.02 (s, 1H, H2), 6.79 (s, 1H, H5), 3.85 (s, 6H, H10, H11), 3,72 (s, 2H, H7), 3,71 (s, 3H, H9) ppm; ¹³C NMR (75 MHz, CDCl₃): δ = 171.4 (C8), 148.9 (C3 or C4), 148.5 (C3 or C4), 126.1 (C6), 115.6 (C2), 115.1 (C1), 114.0 (C5), 56.3 (C10 or C11), 56.2 (C10 or C11), 52.3 (C9), 41.1 (C8) ppm;

IR (film): $v = 2951, 1732, 1506, 1258, 1215, 1161, 1027, 801 \text{ cm}^{-1}$;

HRMS (ESI): calculated for $C_{11}H_{13}O_4^{23}Na^{79}Br^+[M+Na]^+:310.9895$, found: 310.9900.



NaHMDS (2.7 mL of a 2M solution in THF, 5.4 mmol, 1 equiv.) was added dropwise under argon to a solution of the above ester (1.55 g, 5.4 mmol, 1 equiv.) in THF (35 mL). After the reaction mixture had been stirred for 30 min at r. t., MeI (335 μ L, 5.4 mmol, 1 equiv.) was slowly added with a syringe and the reaction mixture was stirred until completion of the reaction. The reaction was quenched with a saturated aq. NH₄Cl solution and the aqueous layer was extracted with Et₂O or AcOEt. The combined organic layers were washed with brine. The extracts were then dried over MgSO₄ and evaporated under reduced pressure. The residue was purified by flash chromatography (heptanes/AcOEt: 9/1) to afford the desired product as a colorless oil (1.39 g, 4.6 mmol, 85% yield). ¹**H** NMR (300 MHz, CDCl₃): δ = 7.01 (s, 1H, H2), 6.82 (s, 1H, H5), 4.15 (q, J = 7.2 Hz, 1H, H7), 3.85 (s, 6H, H11, H12), 3.68 (s, 3H, H9), 1.45 (d, J = 7.2 Hz, 3H, H10) ppm; ¹³**C** NMR (75 MHz, CDCl₃): δ = 174.9 (C8), 148.9 (C3 or C4), 148.7 (C3 or C4), 132.1 (C6), 115.6 (C2), 114.2 (C1), 110.8 (C5), 56.3 (C11, C12), 52.3 (C9), 44.2 (C7), 18.2 (C10) ppm; IR (film): v = 2949, 1731, 1503, 1251, 1207, 1161, 1026, 806 cm⁻¹ HRMS (ESI): calculated for C₁₂H₁₅O₄²³Na⁷⁹Br⁺ [M+Na]⁺: 325.0051, found: 325.0039.

4-(triisopropylsilyloxy)butan-1-ol

HO OH HO 2 4 OTIPS C₁₃H₃₀O₂Si 246,46

According to a described procedure,² a solution of 1,4-butanediol (3.38 g, 37.6 mmol, 1 equiv.) in THF (20 mL) was added dropwise at 0°C to a suspension of NaH (60% in mineral oil, 2.50 g, 37.6 mmol, 1 equiv.) in THF (60 mL). The reaction was stirred for 15 min at 0°C then was warmed to room temperature and stirred for 30 min. TIPSCl (9.92 mL, 37.6 mmol, 1 equiv.) was added portionwise at 0°C. The reaction was then stirred at room temperature for 2h. The reaction mixture was then diluted with Et₂O and H₂O, the two phases were separated and the aqueous layer was extracted with Et₂O. The combined organic layers were washed with a saturated solution of NaHCO₃ and brine, dried over Na₂SO₄. Filtration, evaporation of the solvent and flash chromatography (heptanes/AcOEt 8:2) afforded the monoprotected alcohol (6.94 g, 28.2 mmol, 75% yield) as colorless oil.

¹**H** NMR (300 MHz, CDCl₃): $\delta = 3.74$ (t, J = 5.5 Hz, 2H, H1), 3.66 (d, J = 5.5 Hz, 2H, H4), 2.50 (br s, 1H, OH), 1.70-1.63 (m, 4H, H2, H3), 1.09-1.04 (m, 21H, TIPS) ppm; ¹³**C** NMR (75 MHz, CDCl₃): $\delta = 63.7$ (C1), 63.0 (C2), 30.5 (C3 or C4), 30.2 (C3 or C4), 18.1 (CH_3 TIPS), 12.1 (CH TIPS) ppm; **IR (film):** v = 3335, 2940, 2864, 1462, 1102, 880, 677, 656 cm⁻¹;

HRMS (ESI): calculated for $C_{13}H_{31}O_2^+$ [M+H]⁺: 247.2093, found: 247.2090.

(4-iodobutoxy)triisopropylsilane



Tosylchloride (5.37 g, 18.8 mmol, 1.5 equiv.) was added in one portion at $0^{\circ}C$ to a solution of the above alcohol (4.63 g, 28.2 mmol, 1 equiv.) in pyridine (15 mL). The reaction mixture was stirred at room temperature overnight, and then was diluted with 5% aqueous HCl (70 mL) and extracted with Et₂O. The combined organic layers were washed with a saturated solution of NaHCO₃ and brine, dried over MgSO₄ and the solvent evaporated under reduced pressure, to give the crude tosylate as a yellow oil (5.06 g). The tosylate was then dissolved in acetone (50 mL) containing NaI (11.4 g, 75.8 mmol, 6 equiv.) and stirred at room temperature for 5 h. The mixture was then diluted with H₂O (50 mL) and extracted with Et₂O. The combined organic extracts were washed with a 10% aqueous solution of Na₂SO₃, dried over MgSO₄ and the solvent was evaporated. Flash chromatography (heptanes/diethyl ether: 98/2) afforded the desired product as a colorless oil (3.88 g, 10.9 mmol, 56% yield (2 steps)).

¹H NMR (300 MHz, CDCl₃): δ = 3.71 (t, *J* = 6.2 Hz, 2H, *H4*), 3.69 (t, *J* = 6.9 Hz, 2H, *H1*), 1.99-1.89 (m, 2H, *H3*), 1.68-1.59 (m, 2H, *H2*), 1.07-1.00 (m, 21H, *TIPS*) ppm; ¹³C NMR (75 MHz, CDCl₃): δ = 62.3 (*C4*), 33.8 (*C3*), 30.4 (*C2*), 18.2 (*CH₃ TIPS*), 12.1 (*CH TIPS*), 7.3 (*C1*) ppm;

IR (film): $v = 2939, 2863, 1461, 1103, 880, 678, 656 \text{ cm}^{-1}$;

GC/MS (EI, DB-5ms column, 1 min at 90 °C then 90 \rightarrow 250 °C at 8 °C/min): tr = 14.59 min (*m/z*: 356 [*M*+•]).

² McDougal, P. G.; Rico, J. G.; Oh, Y. I.; Condon, B. D. J. Org. Chem. 1986, 51, 3388.

Methyl 2-(2-bromo-4,5-dimethoxyphenyl)-2-methyl-6-(triisopropylsilyloxy)hexanoate



NaHMDS (1.04 mL of a 2M solution in THF, 2.1 mmol, 1.2 equiv.) was added dropwise at 0 °C to a stirred solution of the above methyl 2-(2-bromo-4,5-dimethoxyphenyl)propanoate (525 mg, 1.7 mmol, 1 equiv.) in freshly distilled THF (35 mL). The mixture was stirred at r. t. for 45 min and was then added via canula to a solution of the above (4-iodobutoxy)triisopropylsilane (926 mg, 2.6 mmol, 1.5 equiv.) in freshly distilled THF (20 mL). After stirring at r. t. for 12h, the reaction mixture was quenched with a saturated aq. solution of NH₄Cl and the aqueous layer was extracted with AcOEt (3 x 20 mL). The combined organic layers were washed with brine (40 mL). The extracts were then dried over MgSO₄ and evaporated under reduced pressure. The residue was purified by flash chromatography (heptanes/AcOEt: 8/2) to afford the desired aryl bromide as a colorless oil (576 mg, 1.1 mmol, 62% yield).

¹**H NMR (300 MHz, CDCl₃):** $\delta = 7.02$ (s, 1H, *H2*), 6.84 (s, 1H, *H5*), 3.87 (s, 3H, *H11 or H12*), 3.85 (s, 3H, *H11 or H12*), 3.68 (s, 3H, *H10*), 3.63 (t, J = 6.5 Hz, 2H, *H16*), 2.27 (dt, J = 13.1, 4.5 Hz, 1H, *H13*), 1.96 (dt, J = 13.1, 4.5 Hz, 1H, *H13'*), 1.59 (s, 3H, *H8*), 1.57-1.46 (m, 2H, *H15*), 1.33-1.20 (m, 2H, *H14*), 0.97 (s, 21H, TIPS) ppm;

¹³**C** NMR (75 MHz, CDCl₃): $\delta = 177.3$ (*C*9), 148.1 (*C*3 or *C*4), 147.9 (*C*3 or *C*4), 134.7 (*C*6), 117.4 (*C*2), 113.9 (*C*1), 111.8 (*C*5), 63.2 (*C*16), 56.5 (*C*11, *C*12), 52.5 (*C*10), 51.1 (*C*7), 36.9 (*C*13), 33.5 (*C*15), 24.3 (*C*14), 20.9 (*C*8), 18.1 (*CH3 TIPS*), 12.1 (*CH TIPS*) ppm;

IR (film): $v = 2941, 1732, 1503, 1246, 1208, 1103, 881, 678 \text{ cm}^{-1}$;

HRMS (ESI): calculated for $C_{25}H_{43}O_5^{23}NaSi^{79}Br^+$ [M+Na]⁺: 553.1961, found: 553.1962.

Benzocyclobutene 2g



A dry resealable Schlenk tube containing a magnetic rod was charged with the above aryl bromide (79 mg, 0.15 mmol, 1 equiv.), palladium acetate (3.3 mg, 0.015 mmol, 0.1 equiv.), tri-*tert* butylphosphine (8.6 mg, 0.030 mmol, 0.2 equiv.), and potassium carbonate (26 mg, 0.19 mmol, 1.3 equiv.). The Schlenk tube was evacuated and backfilled with argon twice, then capped with a rubber septum. Dry N,N-dimethylformamide (0.8 mL) was injected under argon, then the septum was replaced by a screwcap and the mixture was stirred at 140°C (preheated oil bath) for 1h to 1.5h. After cooling, the mixture was diluted with diethyl ether and filtered through Celite®. The organic solution was washed with brine, dried over magnesium sulfate, and concentrated to dryness. The residue was purified by flash chromatography (heptanes/AcOEt: 9/1), and the desired benzocyclobutene **2g** was isolated as a colorless oil (50 mg, 0.11 mmol, 74 % yield).

¹**H NMR (300 MHz, CDCl₃):** $\delta = 6.77$ (s, 1H, *H2*), 6.69 (s, 1H, *H5*), 3.85 (s, 3H, *H11 or H12*), 3.83 (s, 3H, *H11 or H12*), 3.69 (s, 3H, *H10*), 3.67 (t, *J* = 7.0 Hz, 2H, *H16*), 3.53 (d, *J* = 13.4 Hz, 1H, *H8*), 3.00 (d, *J* = 13.4 Hz, 1H, *H8'*), 2.03-1.94 (m, 2H, *H15*), 1.57-1.51 (m, 4H, *H13*, *H14*), 1.05-1.01 (m, 21H, TIPS) ppm;

¹³C NMR (75 MHz, CDCl₃): δ = 175.1 (*C*9), 150.5 (*C*3 or *C*4), 149.7 (*C*3 or *C*4), 138.4 (*C*6), 133.7 (*C*1), 107.5 (*C*2), 106.5 (*C*5), 63.2 (*C*16), 56.3 (*C*11, *C*12), 56.2 (*C*7), 52.1 (*C*10), 40.1 (*C*8), 37.3 (*C*15), 33.2 (*C*13 or *C*14), 22.6 (*C*13 or *C*14), 18.1 (*C*H3 TIPS), 12.1 (*C*H TIPS) ppm; **IR (film):** υ = 2939, 2863, 1730, 1462, 1206, 1103, 880, 678 cm⁻¹;

HRMS (ESI): calculated for $C_{25}H_{42}O_5^{23}NaSi^{79}Br^+[M+Na]^+: 473.2699$, found: 473.2710.



According to the general cycloaddition procedure, benzocyclobutene **2g** (30 mg, 0.07 mmol, 1 equiv.) was reacted with *N*-methylmaleimide (15 mg, 0.135 mmol, 2 equiv.) in *o*-dichlorobenzene (175 μ L) at 180 °C for 15 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 95/5), product **5g** was isolated as a white solid (31 mg, 0.055 mmol, 81% yield).

Mp: 115-116°C;

¹**H NMR (500 MHz, CDCl₃):** δ = 6.89 (s, 1H, *H5*), 6.59 (s, 1H, *H2*), 3.90 (d, *J* = 8.8 Hz, 1H, *H11*), 3.88 (s, 3H, *H17*), 3.83-3.69 (m, 2H, *H21*), 3.81 (s, 3H, *H18*), 3.60 (s, 3H, *H9*), 3.44 (ddd, *J* = 8.8, 7.8, 1.2 Hz, 1H, *H12*), 3.06 (dd, *J* = 15.5, 1.2 Hz, 1H, *H13*), 2.71 (s, 3H, *H16*), 2.67 (dd, *J* = 15.5, 7.8 Hz, 1H, *H13'*), 2.65-2.59 (m, 1H, *H10*), 2.38-2.28 (m, 1H, *H10'*), 1.84-1.65 (m, 3H, *H19, H20*), 1.44-1.25 (m, 1H, *H19'*), 1.16-0.98 (m, 21H, *TIPS*) ppm;

¹³**C** NMR (75 MHz, CDCl₃): δ = 179.6 (C15), 176.8 (C14), 174.0 (C8), 148.5 (C4), 148.2 (C3), 129.1 (C1), 126.7 (C6), 111.7 (C2), 109.2 (C5), 63.4 (C21), 56.1 (C17 or C18), 55.9 (C17 or C18), 52.9 (C9), 52.0 (C7), 43.5 (C11), 40.5 (C12), 33.6 (C19), 33.1 (C10), 29.5 (C13), 24.9 (C16), 21.3 (C21), 18.2 (6 CH_{3TIPS}), 12.2 (3 CH_{TIPS}) ppm;

IR (film): v = 2939, 2863 (v_{C-H}), 1729, 1692, 1681 ($v_{C=O}$), 1440, 1221, 1111, 850, 791, 674, 654 cm⁻¹; **HRMS (ESI):** calculated for $C_{30}H_{47}NO_7^{23}NaSi^+[M+Na]^+$: 584.3020, found: 584.3012.



According to the standard cycloaddition procedure, benzocyclobutene **2h** (35 mg, 0.17 mmol, 1 equiv.) was reacted with *N*-methylmaleimide (38 mg, 0.34 mmol, 2 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C for 20 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 95/5), product **5h** was isolated as a white solid (38 mg, 0.12 mmol, 70% yield). Cristals suitable for X-ray diffraction analysis were grown from heptanes. Crystallographic data for this compound have been deposited with the Cambridge Crystallographic Data Centre under CCDC 707912.

Mp: 152-153°C;

¹**H** NMR (300 MHz, CDCl₃): $\delta = 7.39$ (d, J = 7.6 Hz, 1H, H2), 7.21 (dd, J = 7.6, 7.2 Hz, 1H, H4), 7.20 (dd, J = 7.6, 7.6 Hz, 1H, H3), 7.08 (d, J = 7.2 Hz, 1H, H5), 3.95 (d, J = 9.0 Hz, 1H, H11), 3.61 (s, 3H, H9), 3.46 (ddd, J = 9.0, 8.0, 1.2 Hz, 1H, H12), 3.13 (dd, J = 15.6, 1.2 Hz, 1H, H13), 2.71 (dd, J = 15.6, 8.0 Hz, 1H, H13'), 2.67 (s, 3H, H16), 2.61 (ddd, J = 13.0, 13.0, 5.0 Hz, 1H, H10'), 1.87-1.72 (m, 1H, H17), 1.33-1.19 (m, 1H, H17'), 1.09 (t, J = 7.1 Hz, 3H, H18) ppm;

¹³C NMR (75 MHz, CDCl₃): δ = 179.4 (*C14*), 176.7 (*C15*), 174.1 (*C8*), 137.2 (*C6*), 134.3 (*C1*), 128.6 (*C5*), 128.0 (*C3*), 127.8 (*C4*), 125.4 (*C2*), 53.0 (*C9*), 52.3 (*C7*), 43.6 (*C11*), 40.3 (*C12*), 35.3 (C10), 29.8 (*C13*), 24.8 (*C16*), 18.1 (*C17*), 14.6 (*C18*) ppm;

IR (film): $v = 2963 (v_{C-H})$, 1728, 1685 $(v_{C=O})$, 1214 (v_{C-O}) , 1136, 736 cm⁻¹; **HRMS (ESI):** calculated for $C_{18}H_{21}NO_4^{23}Na^+$ [M+Na]⁺: 338.1368, found: 338.1376.



X-ray crystal structure of compound **5h** (30% ellipsoid plot)



The cycloaddition reaction was performed according to the standard procedure, starting from benzocyclobutene **2i** (22 mg, 0.13 mmol, 1 equiv.) and *N*-methylmaleimide (28 mg, 0.26 mmol, 2 equiv.) in *o*-dichlorobenzene (150 μ L) at 180 °C for 20 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 8/2), product **5i** was isolated as a colorless oil (26 mg, 0.093 mmol, 72% yield).

¹H NMR (300 MHz, CDCl₃): $\delta = 7.34-7.30$ (m, 1H, H5), 7.26-7.22 (m, 2H, H3, H4), 7.15-7.14 (m, 1H, H2), 3.71 (d, J = 9.0 Hz, 1H, H10), 3.69 (dd, J = 15.7, 8.6 Hz, 1H, H12), 3.46 (ddd, J = 9.0, 8.6, 1.6 Hz, 1H, H11), 3.22 (dd, J = 15.7, 1.6 Hz, 1H, H12'), 3.18-3.09 (m, 1H, H9), 2.62 (s, 3H, H15), 1.39 (d, J = 6.5 Hz, 3H, H16 or H17), 1.34 (d, J = 6.5 Hz, 3H, H16 or H17) ppm; ¹³C NMR (75 MHz, CDCl₃): $\delta = 178.3$ (C13), 174.0 (C14), 135.6 (C6), 132.5 (C1), 129.6 (C2), 129.2

(*C3 or C4*), 127.9 (*C3 or C4*), 125.8 (*C5*), 118.6 (*C8*), 47.2 (*C7*), 45.9 (*C10*), 39.9 (*C11*), 30.3 (*C12*), 29.4 (*C9*), 25.0 (*C15*), 21.0 (*C16 or C17*), 19.4 (*C16 or C17*) ppm;

IR (film): $v = 2960 (v_{C-H})$, 2357 $(v_{C=N})$, 1694 $(v_{C=O})$, 1435, 1286 (v_{C-O}) , 1009, 765, 750 cm⁻¹; **HRMS (ESI):** calculated for $C_{17}H_{18}N_2O_2^{23}Na^+ [M+Na]^+$: 305.1266, found: 305.1274.

Synthesis of benzocyclobutene 2j

7-methylbicyclo[4.2.0]octa-1,3,5-triene-7-carboxylic acid



Sodium hydroxide (4.8 g, 124 mmol, 10 equiv.) in water (30 mL) was added dropwise to a stirred solution of the benzocyclobutenecarboxylic ester (2.18 g, 12.4 mmol, 1 equiv.) in methanol (60 mL) at 0°C. The mixture was then refluxed over night. After cooling, aqueous layer was washed with AcOEt, acidified to pH = 2-3 by adding HCl (2N) and extracted with CH_2Cl_2 . The extracts were then dried over magnesium sulfate and evaporated under reduced pressure to afford the corresponding benzocyclobutenecarboxylic acid as a colorless oil (1.84 g, 11.4 mmol, 91% yield).

¹H NMR (300 MHz, CDCl₃): δ =7.27-7.24 (m, 2H, *H2*, *H5*), 7.19-7.12 (m, 2H, *H3*, *H4*), 3.76 (d, *J* = 14.0 Hz, 1H, *H9*), 3.68 (d, *J* = 14.2 Hz, 1H, *H9'*), 1.46 (s, 3H, *H8*) ppm; ¹³C NMR (75 MHz, CDCl₃): δ =181.1 (*C10*), 147.7 (*C6*), 142.4 (*C1*), 128.6 (*C2 or C5*), 127.6 (*C3 or C4*), 123.6 (*C3 or C4*), 121.5 (*C2 or C5*), 52.4 (*C7*), 42.2 (*C9*), 22.7 (*C8*) ppm; IR (film): υ = 3000 (υ _{O-H}), 2969, 2927 (υ _{C-H}), 1692, 1455, 1290, 1174, 734, 710 (υ _{CH ar}) cm⁻¹;

HRMS (ESI): calculated for $C_{10}H_{10}O_2^-$ [M-H]⁻: 161.0603, found: 161.0608.

Benzocyclobutene 2j



Triethylamine (194 μ L, 1.4 mmol, 1.1 equiv.) and diphenylphosphorylazide (DPPA) (280 μ L, 1.3 mmol, 1 equiv.) were added at r. t. to the above benzocyclobutenecarboxylic acid (205 mg, 1.3 mmol, 1 equiv.) in toluene under argon. The resulting solution was heated at reflux for 2h to form the corresponding isocyanate intermediate (isocyanate formation was monitored by GC/MS). The reaction was then cooled to 80°C and allyl alcohol (3 mL) was added via syringe. After 10-12h, the reaction was cooled to r. t. and quenched with a saturated aq. NH₄Cl solution and the aqueous layer was extracted with Et₂O or AcOEt. The combined organic layers were washed with brine. The extracts were then dried over MgSO₄ and evaporated under reduced pressure. The residue was then purified by flash chromatography (heptanes/AcOEt: 9/1), and benzocyclobutene **2j** was isolated as a colorless oil (173 mg, 0.80 mmol, 63% yield).

¹**H NMR (300 MHz, CDCl₃):** δ =7.33-7.28 (m, 3H, *H3*, *H4*, *H5*), 7.17 (d, *J* = 6.8 Hz, 1H, *H2*), 6.00-5.87 (m, 1H, H12), 5.38 (s br, 1H, *NH*), 5.35-5.21 (m, 2H, H13), 4.58 (d, *J* = 5.2 Hz, 2H, *H11*), 3.41 (d, *J* = 14.1 Hz, 1H, *H9*), 3.32 (d, *J* = 14.1 Hz, 1H, *H9'*), 1.77 (s, 3H, *H8*) ppm;

¹³C NMR (75 MHz, CDCl₃): $\delta = 155.4$ (C10), 149.0 (C6), 141.3 (C1), 132.9 (C12), 129.1 (C_{Ar}), 127.4 (C_{Ar}), 124.0 (C2), 121.1 (C_{Ar}), 117.7 (C13), 65.4 (C11), 59.9 (C7), 45.7 (C9), 24.8 (C8) ppm; IR (film): v = 3323 (v_{N-H}), 2926 (v_{C-H}), 1692 ($v_{C=0}$), 1503, 1235, 1081, 1051, 754, 713 ($v_{CH ar}$) cm⁻¹; MS (ES⁺): C₁₃H₁₅NO₂²³Na⁺ [M+Na]⁺: 240.1.

HRMS (ESI): calculated for $C_{13}H_{15}NO_2Na^+[M+Na]^+$: 240.1000, found: 240.0995.



Following the standard cycloaddition procedure, benzocyclobutene **2j** (26 mg, 0.12 mmol, 1 equiv.) was reacted with *N*-phenylmaleimide (20 mg, 0.18 mmol, 1.5 equiv.) in *o*-dichlorobenzene (300 μ L) at 180 °C. After flash chromatography (heptanes then heptanes/AcOEt: 4/2), **5j** was isolated as white solid (26 mg, 0.079 mmol, 67% yield).

Mp: 141-142°C

¹**H NMR (300 MHz, CDCl₃):** δ = 7.38 (dd, *J* = 7.6, 1.2 Hz, 1H, *H5*), 7.29-7.18 (m, 2H, *H3*, *H4*), 7.13 (dd, *J* = 7.2, 1.4 Hz, 1H, *H2*), 6.52 (s br, 1H, *NH*), 6.01-5.90 (m, 1H, *H23*), 5.39-5.22 (m, 2H, *H24*),

4.62-4.59 (m, 2H, *H22*), 3.44 (d, *J* = 8.8 Hz, 1H, *H11*), 3.39-3.32 (m, 1H, H13), 3.26-3.22 (m, 2H, *H12*, *H13'*), 2.82 (s, 3H, *H16*), 1.94 (s, 3H, *H10*) ppm;

¹³C NMR (75 MHz, CDCl₃): δ = 179.2 (*C15*), 177.7 (*C14*), 155.8 (*C9*), 139.7 (*C6*), 133.0 (*C23*), 132.4 (*C1*), 129.3 (*C5*), 128.1 (*C_{Ar}*), 127.8 (*C_{Ar}*), 124.3 (*C2*), 117.9 (*C24*), 65.6 (*C22*), 56.7 (*C7*), 48.7 (*C11*), 38.8 (*C13*), 29.3 (*C12*), 25.2 (*C16*), 25.0 (*C10*) ppm;

IR (film): $v = 3361 (v_{N-H})$, 2945 (v_{C-H}) , 1676 $(v_{C=O})$, 1522, 1436, 1229 (v_{C-O}) , 1058, 763 cm⁻¹; **HRMS (ESI):** calculated for $C_{18}H_{20}N_2O_4^{23}Na^+ [M+Na]^+$: 351.1321, found: 351.1332.



According to the general cycloaddition procedure, benzocyclobutene **2k** (31 mg, 0.11 mmol, 1 equiv.) was reacted with *N*-methylmaleimide (24 mg, 0.43 mmol, 2 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C for 20 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 8/2), product **5k** was isolated as a white solid (41 mg, 0.10 mmol, 95% yield).

Mp: 239-240°C;

¹**H NMR (300 MHz, CDCl₃):** δ = 7.24 (s, 1H, *H5*), 6.65 (s, 1H, *H2*), 3.87 (s, 3H, *H17*), 3.85 (s, 3H, *H18*), 3.85 (d, *J* = 10.0 Hz, 1H, *H11*), 3.84 (s, 3H, *H9 or H19*), 3.72 (s, 3H, *H9 or H19*), 3.33 (ddd, *J* = 10.0, 7.6, 7.6 Hz, 1H, *H12*), 3.05 (dd, *J* = 15.6, 7.6 Hz, 1H, *H13*), 2.95 (s, 3H, *H16*), 2.72 (dd, *J* = 15.6, 7.6 Hz, 1H, *H13*) ppm;

¹³C NMR (75 MHz, CDCl₃): δ = 178.8 (*C15*), 176.5 (*C14*), 169.5 (*C8 or C10*), 168.7 (*C8 or C10*), 149.1 (*C4*), 148.2 (*C3*), 127.6 (*C6*), 124.8 (*C1*), 111.6 (*C2 or C5*), 111.5 (*C2 or C5*), 59.7 (*C7*), 56.2 (*C17 or C18*), 56.0 (*C17 or C18*), 53.8 (*C9 or C19*), 53.4 (*C9 or C19*), 46.9 (*C11*), 39.3 (*C12*), 28.1 (*C13*), 25.2 (*C16*) ppm;

IR (film): $v = 2956 (v_{C-H})$, 1718 ($v_{C=O}$), 1690 ($v_{C=O}$), 1516, 1438, 1267, 1223, 1111, 970 cm⁻¹; **HRMS (ESI):** calculated for $C_{19}H_{21}NO_8Na^+[M+Na]^+$: 414.1165, found: 414.1170.

2. Cycloaddition of various 1,1-disubstituted BCB and activated dienophiles (Table 2)



According to the general cycloaddition procedure, benzocyclobutene **2b** (40 mg, 0.23 mmol, 1 equiv.) was reacted with *N*-phenylmaleimide **4b** (79 mg, 0.45 mmol, 2 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 7/3), **5l** was isolated as a colorless oil (52 mg, 0.15 mmol, 66 % yield).

¹**H** NMR (300 MHz, CDCl₃): $\delta = 7.40-7.26$ (m, 6H, H_{Ar}), 7.18 (d, J = 7.0 Hz, 1H, H2), 6.76 (dd, J = 7.7, 2.0 Hz, 2H, H17, H21), 4.00 (d, J = 8.7 Hz, 1H, H11), 3.67 (s, 3H, H9), 3.61 (ddd, J = 8.7, 7.8, 1.8 Hz, 1H, H12), 3.26 (dd, J = 15.4, 2.0 Hz, 1H, H13), 2.78 (dd, J = 15.4, 7.8 Hz, 1H, H13), 2.05 (s, 3H, H10) ppm;

¹³C NMR (75 MHz, CDCl₃): $\delta = 178.3$ (*C15*), 176.0 (*C14*), 175.5 (*C8*), 137.2 (*C6*), 134.1 (*C1*), 131.7 (*C16*), 129.2 (*C17*, *C21*), 128.8 (*C19*), 128.5 (*C5*), 128.3 (*C2*), 128.0 (*C4*), 126.6 (*C18*, *C20*), 125.5 (*C3*), 53.2 (*C9*), 49.4 (*C7*), 47.2 (*C11*), 40.5 (*C12*), 30.3 (*C13*), 20.8 (*C10*) ppm; IR (film): $v = 2952 (v_{C-H})$, 1728 ($v_{C=0}$), 1703 ($v_{C=0}$), 1391, 1247, 1178, 740, 689 cm⁻¹;

HRMS (ESI): calculated for $C_{21}H_{19}NO_4^{-23}Na^+$ [M+Na]⁺: 372.1212, found: 372.1241.



The cycloaddition reaction was performed according to the general procedure, starting from benzocyclobutene **2c** (40 mg, 0.17 mmol, 1 equiv.) and *N*-phenylmaleimide **4b** (59 mg, 0.34 mmol, 2 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C for 15 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 8/2), **5m** was isolated as a colorless oil (58 mg, 0.14 mmol, 84% yield).

¹**H NMR (300 MHz, CDCl₃):** δ = 7.37-7.29 (m, 3H, *H18*, *H19*, *H20*), 6.89 (s, 1H, *H5*), 6.82 (dd, *J* = 8.0, 1.7 Hz, 2H, *H17*, *H18*), 6.69 (s, 1H, *H2*), 3.97 (d, *J* = 8.9 Hz, 1H, *H11*), 3.90 (s, 3H, *H22*), 3.86 (s, 3H, *H23*), 3.67 (s, 3H, *H9*), 3.59 (ddd, *J* = 8.9, 7.6, 2.0 Hz, 1H, *H12*), 3.19 (dd, *J* = 15.5, 2.0 Hz, 1H, *H13*), 2.72 (dd, *J* = 15.5, 7.6 Hz, 1H, *H13'*), 2.04 (s, 3H, *H10*) ppm;

¹³C NMR (75 MHz, CDCl₃): δ = 178.5 (*C15*), 176.2 (*C14*), 175.5 (*C8*), 148.7 (*C4*), 148.5 (*C3*), 131.7 (*C16*), 129.2 (*C17*, *C21*), 128.8 (*C19*), 126.6 (*C18*, *C20*), 126.4 (*C1*, *C6*), 111.6 (*C2*), 109.2 (*C5*), 56.2 (*C22*, *C23*), 53.3 (*C9*), 49.1 (*C7*), 47.3 (*C11*), 40.7 (*C12*), 30.0 (*C13*), 21.1 (*C10*) ppm;

IR (film): $v = 2930 (v_{C-H})$, 2837, 1704 ($v_{C=O}$), 1504, 1385, 1212 (v_{C-O}), 1192, 1112, 788, 692, 618 cm⁻¹;

HRMS (ESI): calculated for $C_{23}H_{23}NO_6^{23}Na^+[M+Na]^+: 432.1423$, found: 432.1410.



Following the standard cycloaddition procedure, benzocyclobutene **2j** (42 mg, 0.20 mmol, 1 equiv.) was reacted with *N*-phenylmaleimide **4b** (68 mg, 0.39 mmol, 2 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C for 15 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 6/4), **5n** was isolated as a colorless oil (47 mg, 0.12 mmol, 62% yield).

¹**H** NMR (300 MHz, CDCl₃): $\delta = 7.43-7.23$ (m, 6H, H_{Ar}), 7.19 (dd, J = 7.4, 1.5 Hz, 1H, H5), 6.97 (dd, J = 8.0, 1.7 Hz, 2H, H17, H21), 6.53 (s br, 1H, NH), 6.01-5.88 (m, 1H, H23), 5.38-5.19 (m, 2H, H24), 4.62-4.58 (m, 2H, H22), 6.63 (d, J = 9.2 Hz, 1H, H11), 3.56-3.49 (m, 2H, H13), 3.35-3.33 (m, 1H, H12), 2.01 (s, 3H, H10) ppm;

¹³C NMR (75 MHz, CDCl₃): $\delta = 178.3$ (*C15*), 176.6 (*C14*), 155.8 (*C9*), 139.7 (*C6*), 133.0 (*C23*), 132.4 (*C1*), 131.5 (*C16*), 129.3 (*C5*), 129.2 (*C18*, *C20*), 128.9 (*C_{Ar}*), 128.2 (*C_{Ar}*), 127.9 (*C_{Ar}*), 126.5 (*C17*, *C21*), 124.2(*C_{Ar}*), 117.8 (*C24*), 65.6 (*C22*), 56.9 (*C7*), 48.7 (*C11*), 38.9 (*C13*), 29.8 (*C12*), 24.9 (*C10*) ppm;

IR (film): $v = 3351 (v_{N-H})$, 2924 (v_{C-H}) , 1697 $(v_{C=O})$, 1494, 1381, 1246 (v_{C-O}) , 1049, 738, 690 cm⁻¹; **HRMS (ESI):** calculated for $C_{23}H_{22}N_2O_4^{23}Na^+ [M+Na]^+$: 413.1477, found: 413.1477.



According to the general cycloaddition procedure, benzocyclobutene **2a** (50 mg, 0.28 mmol, 1 equiv.) was reacted with maleic anhydride **4c** (56 mg, 0.57 mmol, 2 equiv.) in *o*-dichlorobenzene (250 μ L) at 180 °C under microwave irradiation. After flash chromatography (heptanes then CH₂Cl₂/EtOH: 98/2), **5o** was isolated as a colorless oil (48 mg, 0.17 mmol, 61 % yield).

¹**H** NMR (300 MHz, CDCl₃): $\delta = 7.41-7.32$ (m, 2H, *H5*, *H3*), 7.29 (ddd, J = 7.0, 7.0, 2.0 Hz, 1H, *H4*), 7.17 (d, J = 7.0 Hz, 1H, *H2*), 4.11 (d, J = 9.8 Hz, 1H, *H11*), 3.76 (ddd, J = 9.8, 7.8, 1.9 Hz, 1H, *H12*), 3.64 (s, 3H, *H9*), 3.19 (dd, J = 15.8, 1.9 Hz, 1H, *H13*), 2.76 (dd, J = 15.8, 7.8 Hz, 1H, *H13*'), 2.01 (s, 3H, *H10*) ppm;

¹³C NMR (75 MHz, CDCl₃): δ = 174.6 (*C8*), 173.5 (*C15*), 170.6 (*C14*), 136.3 (*C6*), 133.3 (*C1*), 128.8 (*C5*), 128.8 (*C2*), 128.5 (*C4*), 125.8 (*C3*), 53.5 (*C9*), 48.8 (*C7*), 48.0 (*C11*), 41.0 (*C12*), 29.8 (*C13*), 20.8 (*C10*) ppm;

IR (film): $v = 3022, 2962 (v_{C-H}), 1776 (v_{C=O}), 1715 (v_{C=O}), 1220, 968, 931, 769, 735 cm⁻¹;$

HRMS (ESI): calculated for $C_{15}H_{14}O_5^{23}Na^+$ [M+Na]⁺: 297.0739, found: 297.0753.

GC/MS (EI, DB-5ms column, 1 min at 120 °C then $120 \rightarrow 250$ °C at 8 °C/min): tr = 14.29 min (*m/z*: 274 [*M*+•]).



The cycloaddition reaction was performed according to the general procedure, starting from benzocyclobutene **2c** (50 mg, 0.21 mmol, 1 equiv.) and maleic anhydride (31 mg, 0.32 mmol, 1.5 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C for 15 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 8/2), product **5p** was isolated as a colorless oil (48 mg, 0.14 mmol, 68% yield).

¹**H** NMR (300 MHz, CDCl₃): $\delta = 6.87$ (s, 1H, H5), 6.66 (s, 1H, H2), 4.07 (d, J = 9.7 Hz, 1H, H11), 3.90 (s, 3H, H16), 3.86 (s, 3H, H17), 3.73 (ddd, J = 9.7, 7.6, 1.6 Hz, 1H, H12), 3.64 (s, 3H, H9), 3.11 (dd, J = 15.7, 1.6 Hz, 1H, H13), 2.71 (dd, J = 15.7, 7.6 Hz, 1H, H13'), 1.99 (s, 3H, H10) ppm;

¹³C NMR (75 MHz, CDCl₃): $\delta = 174.6$ (*C8*), 173.7 (*C15*), 170.8 (*C14*), 149.2 (*C4*), 148.9 (*C3*), 128.4 (*C6*), 125.7 (*C1*), 111.8 (*C5*), 109.5 (*C2*), 56.3 (*C16*), 56.1 (*C17*), 53.5 (*C9*), 48.5 (*C7*), 48.1 (*C11*), 41.2 (*C12*), 29.5 (*C13*), 20.9 (*C10*) ppm;

IR (film): $v = 2947 (v_{C-H})$, 2836, 1774 ($v_{C=0}$), 1721 ($v_{C=0}$), 1512, 1218 (v_{C-0}), 1051, 939, 792 cm⁻¹; **HRMS (ESI):** calculated for $C_{17}H_{18}O_7^{23}Na^+ [M+Na]^+$: 357.0950, found: 357.0931.



According to the general cycloaddition procedure, benzocyclobutene **2c** (40 mg, 0.17 mmol, 1 equiv.) was reacted with tetracyanoethylene (44.3 mg, 0.34 mmol, 2 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 7/3), **5q** was isolated as a colorless oil (56 mg, 0.16 mmol, 91% yield).

¹**H NMR (500 MHz, CDCl₃):** $\delta = 6.88$ (s, 1H, H5), 6.62 (s, 1H, H2), 3.91 (s, 3H, H14 or H15), 3.91 (s, 3H, H14 or H15), 3.85 (s, 3H, H9), 3.78 (d, J = 16.9 Hz, 1H, H13), 3.77 (d, J = 16.9 Hz, 1H, H13'), 2.20 (s, 3H, H10) ppm;

¹³**C** NMR (75 MHz, CDCl₃): $\delta = 169.4$ (*C8*), 150.5 (*C3 or C4*), 150.0 (*C3 or C4*), 122.9 (*C6*), 118.4 (*C1*), 111.8 (*C16 or C17*), 111.6 (*C2*), 111.2 (*C16 or C17*), 110.8 (*C5*), 110.3 (*C18 or C19*), 110.3 (*C18 or C19*), 56.4 (*C14 or C15*), 56.2 (*C14 or C15*), 54.2 (*C9*), 52.7 (*C7*), 47.8 (*C11*), 38.4 (*C12*), 37.2 (*C13*), 25.7 (*C10*) ppm;

IR (film): $v = 2958 (v_{C-H}), 2255 (v_{C=N}), 1730 (v_{C=O}), 1523, 1255 (v_{C-O}), 1214, 911, 728 cm⁻¹;$ **HRMS (ESI):** $calculated for <math>C_{19}H_{16}N_4O_4^{23}Na^+ [M+Na]^+$: 387.1069, found: 387.1076.

3. Cycloaddition of 1-monosubstitued BCB 2l (Scheme 3)

The cycloaddition reaction was performed according to the standard procedure, starting from benzocyclobutene **2l** (41 mg, 0.25 mmol, 1 equiv.) and *N*-phenylmaleimide **4b** (87 mg, 0.50 mmol, 2 equiv.) in *o*-dichlorobenzene (200 μ L) at 180 °C for 15 min under microwave irradiation. After flash chromatography (heptanes then heptanes/AcOEt: 8/2), a 1/8 mixture of two diastereoisomers **5ra** and **5rb** was isolated as as a colorless oil (76 mg, 0.23 mmol, 90% yield). Below are reported the NMR signals of major diastereoisomer **5rb**.

¹**H NMR (300 MHz, CDCl₃):** δ = 7.40-7.26 (m, 9H, H_{Ar}), 4.44 (d, J = 5.6 Hz, 1H, H7), 3.52 (s, 3H, H9), 3.27-3.18 (m, 3H, H11, H12, H13), 3.07-2.98 (m, 1H, H13') ppm;

¹³C NMR (75 MHz, CDCl₃): $\delta = 178.5 (C15), 177.5 (C14), 171.5 (C8), 136.7 (C1), 133.2 (C6), 132.4 (C3), 129.6 (C_Ar), 129.3 (C18, C20), 128.8 (2 C_Ar), 128.7 (C_Ar), 127.8 (C_Ar), 126.9 (C17, C21), 52.8 (C9), 46.8 (C7), 41.9 (C11), 39.6 (C12), 28.5 (C13) ppm;$

IR (film): $v = 2950 (v_{C-H})$, 1706 $(v_{C=O})$, 1492, 1381, 1212 (v_{C-O}) , 1085, 758, 741 cm⁻¹; **HRMS (ESI):** calculated for $C_{20}H_{17}NO_4^{23}Na^+ [M+Na]^+$: 358.1055, found: 358.1087.